



DEPARTMENT OF HEALTH & HUMAN SERVICES

Food and Drug Administration  
New England District

2/17/01

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Stoneham, Massachusetts 02180  
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September 6, 2001

**WARNING LETTER**

**NWE-38-01W**

**VIA FEDERAL EXPRESS**

James F. Miller, President  
Bindley Western Industries, Inc.  
7000 Cardinal Place  
Dublin, OH 43017

Dear Mr. Miller:

The Food and Drug Administration (FDA) conducted an inspection of your wholesale prescription drug distribution facility at 5 Bradley Drive, Westbrook, Maine between January 30 and February 16, 2001. At the conclusion of that inspection the FDA investigator issued a Form FDA 483 (Inspectional Observations). This form listed the conditions or practices observed by the investigator during the inspection that represent significant deviations from the requirements of Section 501(a)(2)(B) of the Federal Food, Drug, and Cosmetic Act (the Act) [21 U.S.C. 351(a)(2)(B)] and the Guidelines for State Licensing of Wholesale Prescription Drug Distributors, established by regulation at Title 21, Code of Federal Regulations, Part 205 (21 CFR Part 205), promulgated pursuant to Sections 503(e)(2)(A) and (B) of the Act [21 U.S.C. 353(e)(2)(A) and (B)].

The significant deviations noted during the inspection include, but are not necessarily limited to, the following:

- 1) Returning to the marketplace drug products that had been subjected to improper storage conditions, including extremes in temperature, contrary to the requirements of Parts 205.50(e)(3) and 205.50(j) of Title 21 of the Code of Federal Regulations (21 CFR § CFR 205.50(e)(3); 21 CFR § 205.50(j)). For example,

On December 26, 2000 your firm learned from one of your customers that a large portion of a shipment of [REDACTED] vials of Hepatitis B Vaccine (Recombinant) Engerix-B® Lot ENG3382A4 had arrived at its destination in a

frozen state. This shipment was returned to your Westbrook, Maine facility. Despite unambiguous instructions on the product labeling ( "Store refrigerated between 2° and 8° C (36° and 45° F). Do not freeze. Discard if frozen" ), the returned product was placed into active inventory and sale of the product was resumed. Your justification for this action was based on a verbal authorization from the vaccine's manufacturer following an inspection by the manufacturer of a sample from this shipment that you provided. However, your firm merely stated that the freeze indicators had been activated, and did not inform the manufacturer that your customer had reported that product may actually have been frozen during shipment. The manufacturer's follow-up letter to you mentions nothing more than a physical evaluation of the product in response to a complaint that the cold indicators had been activated.

- 2) Failure to assure that all prescription drugs are stored at appropriate temperatures and under appropriate conditions in accordance with requirements in the labeling of such drugs, as required under 21 CFR § 205.50(c). For example,
  - a) The reserve cooler and picking cooler were observed to be operating with temperature alarm set points of [REDACTED] (lower limit) and [REDACTED] (upper limit). However, at least three products distributed by your firm were noted to have labeled storage conditions of (not lower than) 36° F and (not more than) 46° F.
  - b) No corrective measures were taken when continuous temperature recording charts for the picking cooler showed temperature readings below 36° F during 5 consecutive weekly monitoring periods from November 20, 2000 through January 7, 2001.
  - c) No corrective actions were taken as a result of numerous instances of alarm activity for the picking cooler between November 25, 2000 and February 14, 2001.
- 3) Failure to assure that drug products are held under conditions that are in conformance with storage requirements set for those drugs, in violation of Section 501(a)(2)(B) of the Act. For example:

Temperature monitoring and alarm systems for refrigeration units were not validated for the required storage ranges of drug products stored therein. Specifically, your refrigeration units were observed to be capable of operating outside of the storage ranges set for Hepatitis B Vaccine (Recombinant) Engerix-B®, Tetanus and Diphtheria Toxoids Adsorbed For Adult Use, and Diltiazem Hydrochloride Injection, all of which are routinely stored in these units.

- 4) Failure to consider the conditions under which a drug has been held, stored, or shipped before or during its return, as required under 21 CFR § 205.50(e)(3). For example,

Prescription drugs, including temperature-sensitive products such as vaccines, are delivered from your facility to your customers using two contracted delivery services, which employ unrefrigerated trucks. Whenever your customers return product to your facility, these same delivery services are used. Moreover, the returned product is not delivered directly to your Westbrook warehouse, but is instead held by the delivery service until it is retrieved by your personnel. This practice, in and of itself, results in conditions that cast doubt on the quality of products that require controlled refrigerated storage, regardless of any written documentation provided by the customer showing that proper storage conditions have been maintained.

- 5) Failure to establish, maintain, and adhere to written policies and procedures concerning the following, as required under 21 § CFR 205.50(g):

- Monitoring of the temperature recording records of the refrigeration units used to store drug products, in order to identify temperature excursions, to document corrective actions, and to document actions that are taken to dispose of drug products held outside of their labeled storage temperature requirements.
- Preparation and packaging for shipment, so that labeled storage temperature conditions are met during transit.
- Examination of incoming drug products, to assure that labeled storage temperature conditions are met during transit.
- Failure to follow a Standard Operating Procedure (SOP) that requires customers, who return drug products to sign a certification that the drug products were stored under appropriate conditions. Specifically, on two occasions customers were observed to have returned drug products without a signed certification

We have received the letter from John C. Erickson III, Senior Compliance Counsel, which is dated February 22, 2001 and was sent in response to the Form FDA 483 (Inspectional Observations) that was issued by our investigator at the conclusion of the inspection.

Your responses to Form FDA 483 items 10, 11, and 12 appear to be adequate.

Your responses to Form FDA 483 items 1 through 6 (reiterated as Warning Letter items 2(a) – (c)), if fully implemented, appear to adequately address the inspectional observations. However, I would strongly encourage you to submit any documentation

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that may have been developed as a result of the February 22 meeting you reported holding with the vendor of the monitoring and alarm systems for the refrigerated storage units.

However, with regard to the issue of refrigerated storage of product during shipment, which is mentioned in Form FDA 483 observations 7, 8, and 9 (reiterated as Warning Letter items 1 and 3), your response is less than adequate, for the following reasons:

- Item 15 of Procedure PDMA-1 *Receiving Prescription Drugs* states that items requiring refrigeration must be delivered promptly to the refrigerator receiving area. However, no provisions appear to exist to check for products that may have been frozen during shipment.
- Item 11 of Procedure PDMA-4 *Order Filling* states merely that orders are loaded onto delivery trucks. There are no explicit measures described which would ensure that product is not subjected to temperature abuse (including freezing) during transit.
- Procedure PDMA-6 *Distribution and Delivery* appears to be directed to Cardinal (Bindley) personnel. Your firm currently relies upon contract delivery services to ship customer orders and retrieve product that is being returned. Once again no specific provisions appear to have been included for the possibility of product freezing during shipment.

The violations identified above are not intended to be an all-inclusive list of deficiencies at your facility. It is your responsibility to ensure adherence to all applicable regulations and provisions of the Act. Federal agencies are advised of the issuance of all Warning Letters about drugs and medical devices, so that they may take this information into account when considering the award of contracts.

You should take prompt action to correct these deviations. Failure to promptly correct these deviations may result in regulatory action without further notice. Possible actions include seizure and or injunction. Insofar as the deficiencies noted at your Westbrook, Maine facility may be symptomatic of underlying quality assurance problems, similar deficiencies may also exist at other sites. This letter is intended to serve as official notice that FDA expects compliance at all of your facilities.

A copy of the Form FDA 483 (Inspectional Observations) that was issued to Mr. George S. Vecchia, Vice President, Division Manager, Bindley Western Drug Company, Westbrook, ME is enclosed for your reference.

A copy of this Warning Letter has been sent to the Maine Board of Pharmacy, Office of Licensing and Registration for their information and follow-up.

You should notify this office in writing, within fifteen (15) working days of the receipt of this letter, of the specific steps you have taken to correct the noted violations, including

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an explanation of each step being taken to prevent the recurrence of similar violations. If corrective action cannot be completed within 15 working days, state the reason for the delay and the time within which corrections will be completed.

Your response should be sent to Mark Lookabaugh, Compliance Officer, U.S. Food and Drug Administration, One Montvale Avenue, 4th Floor, Stoneham, MA 02180. If you have any questions concerning this matter, please contact Mr. Lookabaugh at 781.596.7751.

Sincerely,

  
Gal T. Costello  
Director  
New England District

Enclosure

cc (without enclosure):

George Vecchia  
Vice President, Division Manager  
Bindley Western Drug Company  
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Westbrook, ME 04092

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